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Reversible, Solvent-Induced Chirality Switch in Atrane Structure: Control of the Unidirectional Motion of the Molecular Propeller

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Abstract: Here we demonstrate that atrane−hemicryptophane molecular cages exhibit a reversible change in chirality uniquely controlled by the solvent, thus establishing the feasibility of a new mode of stimulation for atrane-based molecular switches. The oxidovanadium(V) complexes of hemicryptophane molecules exist as diastereomeric mixtures because of the *P* or *M* handedness of the cyclotriveratrylene unit and the chiral ether groups with the *S* configuration. The Δ/Λ propeller-like arrangement of the atrane moiety introduces a new local dissymmetry because of the conformationally restricted helical structure. ^{1}H NMR experiments provided significant data for the Δ ⇆ Λ interconversion process, where the solvent profoundly influences the chirality sense of the propeller motion, making control of the chirality by the choice of solvent possible. The reversible chirality inversion process is induced by alternating changes of solvent from $CDCl_3$ to C_6D_6. The ratio of the rates of the clockwise and anticlockwise tilting motions of the atrane structure shows that the solvent directs the rotational motion of the vanatrane moiety, so the propeller sense of the motion can be considered as unidirectional.

There is an increased interest in the synthesis and development of systems capable of performing a defined function at the molecular level.[1] Among them, molecular switches can change reversibly between two stable states under the action of external chemical, electrochemical, photochemical, or thermal input.[2] Nevertheless, generating systems capable of directional motion at the molecular level is still a challenge.[3] It is essential that switch elements operate above randomness, and the system has to be bistable. In that context, conformational interchange of flexible molecular structures controllable by external stimuli that induces a reversible change in chirality are particularly attractive. Many chirality switches have been described, but only a few systems show a unidirectional movement caused by a change of configuration or conformation.[4] Here we demonstrate the reversibility of a uniquely solvent-controlled chirality switch in molecular cages bearing an atrane structure.

Atrane derivatives with a C_3-symmetrical backbone are an interesting class of compounds because they exhibit Δ and Λ mirror-image conformations, which adopt the right- and left-handed propeller geometry, respectively.[5] For instance, the vanatrane derivatives obtained from the triethanolamine core and oxidovanadium(V) complexes furnish Λ/Δ enantiomers as depicted in Figure 1. Thus, if it is controllable by external stimuli, the unidirectional tilting of the three fused five-membered rings can furnish a right- (Δ) or left-handed (Λ) conformer. Introduction of appropriate chirogenic elements can potentially bias the interconversion process to favor one propeller sense over the other. These two forms could in principle be used as a reversible bistable system in which control of the motion direction of the propeller could be achieved.

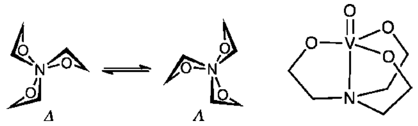
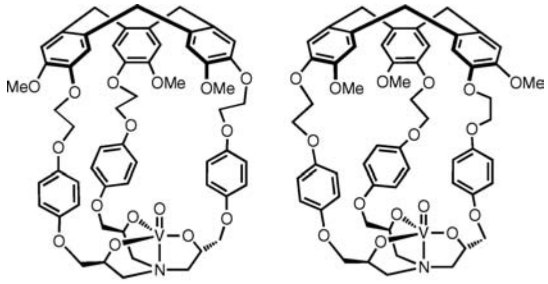


Figure 1. (right) Vanatrane structure and (left) its Δ and Λ forms (viewed down the N−V bond).

C_3-symmetrical oxidovanadium(V) complexes of hemicryptophane molecules exist as diastereomeric mixtures because of the *P* or *M* handedness of the cyclotriveratrylene unit (CTV) and the chiral ether groups with the *S* configuration (Figure 2).[6] The diastereomerically pure chiral complexes **1** and **2** can exist as two diastereomeric conformers, (Λ)-**1**/(Δ)-**1** and (Λ)-**2**/(Δ)-**2**, corresponding to the Λ and Δ forms of the vanatrane moieties.[7] The Λ ⇆ Δ stereoconversion between clockwise and anticlockwise orientations of the helical arrangement exhibited an unexpectedly high energy barrier and proved to be strongly solvent-dependent. This interconversion process could potentially function as a reversible molecular switch controlled by the solvent, which can strongly affect the Λ/Δ ratio and lead to predominance of one diastereomer over the other, providing a means of controlling the chirality sense in the molecule.



M-(SSS)
1

P-(SSS)
2

Figure 2. Structure of the diastereomers **1** [*M*-(*S*,*S*,*S*)] and **2** [*P*-(*S*,*S*,*S*)], each of which exists in Λ and Δ forms [(Λ)-**1**/(Δ)-**1** and (Λ)-**2**/(Δ)-**2**, respectively].

We first investigated the reversibility of the switch using ^{1}H NMR spectroscopy (see the Supporting Information). The Λ/Δ ratio of a (Λ)-**1**/(Δ)-**1** mixture in C_6D_6 solution decreased from 1/0.35 to 1/1 as a result of interconversion between the two conformers of diastereomer **1**. At thermodynamic equilibrium, the solvent was evaporated, and the solid was dissolved in $CDCl_3$. An increase in the Λ/Δ ratio from 1/1 to 1/0.35 was observed. Therefore, alternating changes in the solvent resulted in a diastereoselective interconversion between the two stable states having (Λ)-**1**/(Δ)-**1** ratios of 74/26 and 50/50, respectively (Figure 3a). A 26% difference in the population of the solvent-dependent states and reversal of the helicity were achieved, and it was possible to perform at least six switching cycles, leading to a reversible bistable system. The same experiment run with the (Λ)-**2**/(Δ)-**2** mixture led to a less pronounced diastereo-

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selective interconversion [85/15 and 97/3 (Λ)-**2**/(Δ)-**2** ratios in $CDCl_3$ and C_6D_6, respectively] (Figure 3b). In that case, we also demonstrated the reproducibility of the system by performing six switching cycles. This demonstrated that atrane propellers are a new class of chiral bistable systems capable of switching reversibly with external stimuli. It can be noticed that each state can be read in a nondestructive manner using ^{1}H NMR spectroscopy.

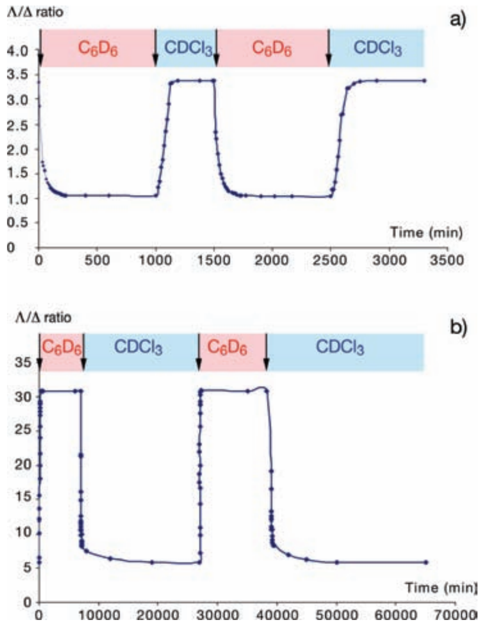

Figure 3. Plot of the Λ/Δ ratio (from ^{1}H NMR data) vs time for the Λ $\leftrightarrows$ Δ stereoconversion, after alternating dissolution in C_6D_6 and $CDCl_3$: (a) (Λ)-**1** $\leftrightarrows$ (Δ)-**1**; (b) (Λ)-**2** $\leftrightarrows$ (Δ)-**2**.

Next, we studied more accurately the control of the molecular switch on the rotational motion by following the rates of the clockwise and anticlockwise motions of the atrane moiety by ^{1}H NMR spectroscopy. In $CDCl_3$ the Λ/Δ ratio of a 1/1 (Λ)-**1**/(Δ)-**1** mixture increased from 1/1 to 1/0.35, accounting for a preferential anticlockwise rotational motion. The time evolution of the ratio of the rate of the clockwise motion to that of the anticlockwise motion is shown Figure 4. The anticlockwise direction of motion is more favored at the beginning of the dissolution since it is under far-from-equilibrium conditions. It becomes less and less predominant as time passes, and finally, the two directions of motion are equally favored at equilibrium, as they have the same rate.

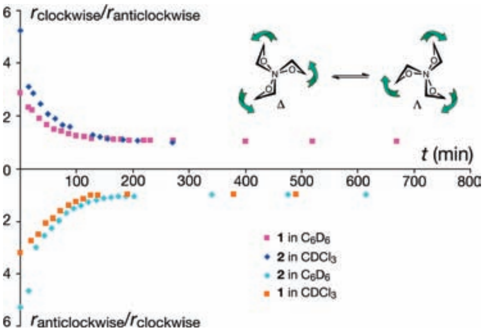

Figure 4. Ratios of the rates *r* of the clockwise and anticlockwise motions as functions of time for **1** and **2** in $CDCl_3$ and C_6D_6.

The same experiment performed with a 1/0.17 (Λ)-**2**/(Δ)-**2** mixture in C_6D_6 resulted in an increase of the Λ/Δ ratio from 1/0.17 to 1/0.03, accounting for a preferential anticlockwise motion. As expected, the ratio of the rate of the anticlockwise motion to that of the clockwise motion decreased with time. These experiments prove that the solvent could determine the direction of the rotational motion of the vanatrane derivatives. Additionally, Figure 4 shows that for both diastereomers, changing the solvent led to a preferential clockwise motion.

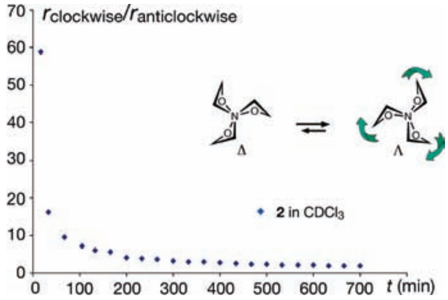

Figure 5. Ratio of the rates of the clockwise and anticlockwise motions as a function of time for crystals of (Λ)-**2** in $CDCl_3$ solution.

To improve the control over the rotational motion, single crystals of the pure (Λ)-**2** isomer were dissolved in $CDCl_3$. The ^{1}H NMR spectrum of the (Λ)-**2** diastereomer at 298 K slowly evolve, and at equilibrium, a 1/0.17 ratio was measured for the two diastereomers (Λ)-**2** and (Δ)-**2**. The ratio of the rate of the clockwise motion to that of the anticlockwise motion as a function of time is shown in Figure 5. As expected, under these far-from-equilibrium conditions [short time and negligible (Δ)-**2** concentration], the rate of the clockwise motion was increased. For example, the rate of the clockwise motion was 60-fold higher than that of the anticlockwise motion at $t = 17$ min and was still 10-fold higher after 60 min. Thus, at short times, the rotational motion can be considered unidirectional.

In conclusion, we have demonstrated that both vanatrane structures **1** and **2** constitute bistable systems that can reversibly interconvert by means of an unusual external stimulus: the solvent. The conversion of the propeller-like hemicryptophane complexes leads to the clockwise−anticlockwise Λ $\leftrightarrows$ Δ rearrangement. Hence, the atrane structure appears to undergo a chirality switch. The solvent controls the direction of the tilt, and the ratio of the stereoconversion rates can be tuned by the initial Λ/Δ ratio. Therefore, a quasi-unidirectional motion of the propeller atrane moiety can be observed. This class of atrane propellers is for the first time exploited as a novel mode of switching that is worthy of being explored for potential applications.

Supporting Information Available: Experimental details and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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